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Highlights

- Applying cluster analysis, Lysaker et al. (2004), identified different subgroups of schizophrenia patients with and without OCS, those with relatively high social functioning and those with relatively low social functioning. The current study is a replication approach in a large representative cohort of patients with psychotic disorder with cross-sectional and longitudinal assessments.
- Similar to the study of Lysaker et al. (2004) cluster analysis formed subgroups differing in the presence of OCS and social functioning. In the current study the following five clusters were identified: an OCSneg/HF (no OCS/ high functioning) group, an OCSneg/PF (no OCS/poor functioning) group, an OCSmild/HF (mild-OCS/ high functioning) group, an OCSmild/PF (mild-OCS/ poor functioning) group and an OCShigh/MF (high-OCS/ moderate functioning) group.
- In line with the study of Lysaker et al. (2004), the OCSmild/HF group showed less negative symptoms than the poor functioning groups. However, in contrast to the original study, the group with OCS and poor functioning did not differ in executive functioning or sustained attention compared to the other groups.
- Results support the idea that co-morbid OCS can have different implications for different subgroups of patients.

Patterns of obsessive-compulsive symptoms and social functioning in schizophrenia; a replication study

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Abstract

Research has found that Obsessive Compulsive Symptoms (OCS) in schizophrenia are associated with either more or less negative symptoms and either better or poorer cognitive functioning. In order to explain these contradictory results, Lysaker et al.(Lysaker et al., 2004), performed a cluster analysis resulting in 2 OCS positive (OCSpos) clusters, one with higher functioning (HF) and one with poorer functioning (PF) compared to 2 OCS negative (OCSneg) clusters. The OCSpos/HF cluster had less negative symptoms compared to all other clusters, while the OCSpos/PF cluster showed poorer executive functioning. We performed a replication study, in an almost 10 times larger, representative sample, using both a longitudinal and cross-sectional design. Similar to Lysaker et al., we found a group with mild OCS and HF (OCSmild/HF) showing less negative symptoms compared to the PF groups. We also found an OCSmild/PF group, which did not significantly differ in executive functioning from the other groups. Moreover, we did not find evidence for a better prognosis in the OCSmild/HF group, and thus found no support for the assumption that for some patients OCS might be an effective coping mechanism.

1. Introduction

The co-occurrence of obsessive compulsive symptoms (OCS) and obsessive compulsive disorder (OCD) in schizophrenia has been studied extensively over the past three decades. Until the 1980's OCD was believed to be a rare condition in schizophrenia with incidence rates varying from 1.1% to 3.5% in studies of clinical records (Rosen, 1957). Jahrreiß and Rosen concluded that patients with schizophrenia and comorbid OCD "tended to have a comparatively benign clinical course and better outcome" (Hwang et al., 2006). Recently, a meta-analyses found a mean OCD prevalence of 12.3% in patients with schizophrenia. Obsessive-compulsive symptoms (OCS) were reported in 30.7% of cases (Swets et al., 2014). Moreover, contrary to what Jahrreiß and Rosen concluded, many studies found that comorbid OCD in schizophrenia patients was associaded with poorer social functioning (de Haan et al., 2012; Fenton and McGlashan, 1986), more severe positive and negative symptoms and lower global functioning (Berman et al., 1998; Cunill et al., 2009; Hwang et al., 2000; Lysaker et al., 2000; Schirmbeck et al., 2016b). However, some studies found less severe negative symptoms in patients with comorbid OCS (Tibbo et al., 2000), lower levels of positive and negative symptoms in patients with a first psychotic episode and comorbid OCS (de Haan et al., 2005; Poyurovsky et al., 1999) or less formal thought disorders (Bleich-Cohen et al., 2014), while others found no significant association between OCS and other symptoms (de Haan et al., 2012; Faragian et al., 2009; Nasrollahi et al., 2012; Poyurovsky et al., 2006). Inconsistent findings have also been reported regarding assoiations between comorbid OCS and cognitive functioning in patients with psychotic disorders (Meijer et al., 2013; Schirmbeck et al., 2016a) and in the at risk mental state (Zink et al., 2014). In an attempt to explain these discripancies in clinical findings, several authors postulated that patients with schizophrenia and OCS might represent distinct subgroups (de Haan and Zink, 2015; Schirmbeck et al., 2015). Whereas some authors proposed subgroups according to differences in neurobiological features or antipsychotic treatment (Schirmbeck and Zink, 2013), Lysaker et al. hypothesized two distinct groups in patients with schizophrenia and comorbid OCS based the phenomenological level, one associated with poorer functioning and worse outcome, the other with better functioning and better

outcome (Lysaker et al., 2004). Identification of these subgroups would partially explain the heterogenity in outcome and would give support to earlier findings that OCS is associated with a benign course in some individuals. Lysaker and colleagues performed a cluster analysis using the Yale Brown Obsessive and Compulsive Scale (Y-BOCS; (Goodman et al., 1989)) to asses OCS and the Quality of Life Scale (QoL) (Heinrichs et al., 1984), to assess psycho-social functioning. Cluster analysis assigns patients to a group in such a way that patients in the same group (called a cluster) are more similar to each other than the patients in the other clusters. Lysaker et al. analysed different cluster solutions and identified 4 cluster as the optimal solution. This solution consisted of a poor functioning (PF) and a high functioning (HF) group with OCS (OCSpos) and a PF and a HF group without OCS (OCSneg). The OCSpos/HF group had less severe negative symptoms than all the other groups, whereas the OCSpos/PF group showed poorer attention and executive functioning compared to the other groups. Positive symptoms did not differ significantly between the groups. From this study it appeared that OCS was associated with better functioning in some individuals and with poorer functining in others when compared to the OCSneg groups. These different subgroups might have clinical implications as to how co-morbid OCS in schizophrenia should be interpreted and treated. However, the study sample of Lysaker et al. was small, with a total sample of 66 patients, and groups consisting of 9-25 individuals. Hence, findings of this study need replication in a larger sample. The Genetic Risk and Outcome of Psychosis (GROUP) study sample is a large representative cohort of patients with non-affective psychotic disorders, who have been extensivly investigated regarding different aspects of functioning and psychopathology, both cross-sectionally and longitudinally.

In this paper we aim to replicate the cluster analyses of Lysaker et al. (2004), in the large GROUP sample, using both a cross-sectional and longitudinal design. Similar to Lysaker et al., we expect to distinguish four subgroups of patients with schizophrenia and comorbid OCS: one with good social functioning and one with poor social functioning and comparable subgroups in patients with

schizophrenia without OCS using cluster analysis. In line with their findings, our primary hypotheses are a) that patients in the OCSpos/PF group will show poorer executive functioning and sustained attention and more negative symptoms than any other group and b) that patients in the OCSpos/HF group will show lower levels of negative symptoms compared to the poor functioning groups. Furthermore, in a longitudinal approach we will evaluate whether proposed differences in cognitive domains and negative symptoms between clusters, will remain present at 3 year follow-up. As Lysaker et al. (2004) suggested in their discussion: "research employing longitudinal assessments of the fate of patients with and without OCS symptoms will shed more light on the question if subgroups exist". Stability of outcome will favour this hypothesis. More specifically, we will test the hypothesis c) that differences in negative symptoms and cognitive functioning between the four subgroups at baseline remain stable at 3-year follow-up.

2. Methods

2.1. Study design and participants

The study sample was part of the multicenter GROUP study. The procedure of recruitment and population characteristics have been described in detail elsewhere (Korver et al., 2012). In short, inclusion criteria for patients were (1) age range of 16 to 50 years and (2) good command of the Dutch language. Patients had to meet DSM-IV-TR criteria for a non-affective psychotic disorder (APA, 2000) which was assessed with the Comprehensive Assessment of Symptoms and History (CASH (Andreasen NC, 1992)) or the Schedules for Clinical Assessment for Neuropsychiatry version 2.1 (SCAN (Wing JK, 1990)). GROUP participants were included in a post-acute phase, when they were willing and able to take part in assessments lasting on average four hours. All participants provided written informed consent prior to their inclusion in the study, which was approved by the accredited Medical Ethics Review Committee (METC). Patients with complete data on the Y-BOCS and the Social Functioning Scale (SFS) (n=655) were included in the current study.

2.2. Clinical Measures

Sociodemographic and clinical data on age, gender, education level, duration of illness, IQ estimation (Korver et al., 2012) and medical treatment were included in the current study.

Severity of OCS was measured with the Y-BOCS (Goodman et al., 1989). The Dutch translation of the YBOCS has been validated for the assessment of OCS in schizophrenia (Boyette et al., 2011; de Haan et al., 2006). The Y-BOCS assesses different aspects (time, handicap, frequency, controllability, and discomfort) of obsessions compulsions on 5-point Likert-scales, resulting in two subscales and a total score. Severity of positive, negative symptoms and general psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS) according to the three-factor model (Kay et al., 1987). The PANSS has been translated into Dutch by Linszen, de Haan, Kuipers and Dingemans, AMC department of psychiatry (1995).

In accordance to Lysaker et al. (2004) the two cognitive domains of executive functioing and sustained attention were investigated (Lysaker et al., 2004). Impairment in executive functioning and flexibility in thought was assessed with the Response shifting task (RST) a modified version of the Competing Programs Task (Nolan et al., 2004). Sustained attention was measured with the Continuous Performance Test (CPT) (Nuechterlein and Dawson, 1984). For both tasks, assessment was computerized using E-prime 1.3 (Psychology Software Tools, Inc., Pittsburgh, PA, 2001). In addition to tasks assessing executive functioing and sustained attention we also included the Digit-Symbol Coding test (DSC), a subset of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III (Wechsler, 1997)) measuring processing speed in a visual perception and memory task. The Dutch translation of the WAIS-III has been validated by van der Heijden (2013)(van der Heijden et al., 2013). Performance in this task has been found associated with co-occurring OCS in previous studies (Meijer et al., 2012; Schirmbeck et al., 2016a).

The SFS (Birchwood et al., 1990) was used to assess social functioning over the past 3 months. The scale was translated into Dutch by de Boer et al. (2002) in agreement with the original

authors. The SFS has been widely used to measure areas of functioning essential for successful community maintenance, containing 7 subscales: withdrawal, interpersonal behavior, prosocial activities, recreation, independence-performance, independence-competence, and employment/occupation. The SFS has shown to be a reliable and valid measure in both patients with psychotic disorders and the general population (Birchwood et al., 1990). Higher scores on the SFS indicate higher levels of social functioning. We used the overall score in the analyses.

The Global Assessment of Functioning-symptoms (GAF S) (Jones et al., 1995) was used to assess the severity of symptoms in combination with functioning. The GAF is a widely used assessment instrument with scores ranging from 0 to 100, with higher scores corresponding with less symptoms. The Dutch version of the GAF is part of the DSM-IV-TR (APA, 2000) and has been validated in Dutch patients (*Havenaar et al.*, 2004).

2.3. Statistical analysis

We performed Statistical analyses using the Statistical package for Social Sciences (SPSS version 24.0, Chicago, IL, US). According to Lysaker et al (2004), cluster analysis was based on assessment instruments measuring OCS and social functioning. Therefore, Y-BOCS and SFS scores were transformed to z-scores. Average between group linkage hierarchical cluster analysis was used to determine the optimal number of clusters, using the squared Euclidian distance. An optimal number of clusters is reached when as few as possible clusters with an minimum distance to the mean is identified. The number of clusters before a jump in coefficient values is generally considered as the optimal (Yim, 2015). Subsequently we performed K-Means cluster analyses to determine the Y-BOCS and SFS scores of the clusters, the patient subgroups. After the clusters were defined, Pearson Chi-Square tests and t-tests were used when appropriate, in order to determine demographic, illness characteristics and prevalence of the different clusters. Analyses of covariance (ANCOVA) was used to compare the identified clusters on psychopathology as measured with the PANSS and cognitive domains as measured with the RST accuracy scores, the

CPT omission and commission scores and the DSC task, corrected for significant covariates and using Bonferroni correction. Release 5.0 of the GROUP database was used for the analyses.

3. Results

Hierarchical cluster analyses were performed (n=655) to investigate if we can replicate the proposed four subgroups of patients with schizophrenia and comorbid OCS: one with good social functioning and one with poor social functioning, and comparable subgroups in patients with schizophrenia without OCS. Following Lysaker et al. (2004), we focused on the optimal solution looking at 2-6 possible clusters, and identified the 4 cluster solution as optimal after examination of the Euclidian squared distances between the clusters. However, this 4 cluster solution yielded 3 OCSpos groups and only one OCSneg group, making good comparison with the groups identified by Lysaker et al.(2004) impossible. The 5 cluster solution (with a faily similar squared Euclidian distance) resulted in comparable subgroups with high and poor functioning in both groups with and without co-morbid OCS, hence we decided to use the 5 cluster solution.
Table 1 shows mean SFS and Y-BOCS scores, demographic characteristics and clinical variables of the 5 clusters. Cluster n=276 participants with OCSneg/HF (no-OCS and high functioning), cluster 2 n=52 participants with OCSmild/HF (mild OCS and high functioning), cluster 3 n=36 participants with OCShigh/MF (high OCS and moderate functioning), cluster 4 n=241 participants with OCSneg/PF (no-OCS and poor functioning), cluster 5 n=50 participants with OCSmild/PF (mild OCS and poor functioning). Gender, IQ and clozapine use differed significantly between groups and were added as covariates in subsequent group comparisons.

To evaluate the proposed differences in cognitive domains and negative symptoms between the subgroups, analyses of covariance were performed. Cross-sectionally, ANCOVA revealed significant differences between groups on DSC scores and CPT omission scores. Groups did neither significantly differ on RST accuracy scores nor on CPT commision scores. Pairwise comparison did not reveal significant differences on CPT omission scores. Regarding the DSC, the only significant

group differences were found for better performance of the OCSneg/HF group compared to the two poor functioing groups (see table 2).

Regarding negative symptom severity, analysis revealed a significant overall group effect. Subsequent pairwise comparisions showed that the OCSmild/HF group had significantly lower scores compared to the two PF groups. Compared to the other two groups there was no significant difference in PANSS-negative scores. The OCSmild/PF did not differ from the OCSneg/PF, but showed lower scores than the two HF groups. In addition, the OCSneg/HF group showed less positive and general symptoms compared to all other groups and the OCShigh/MF group showed higher positive and general symtpoms compared to all other groups, except for the OCSmild/PF group (see table 2). When including covariate in the analyses, the results did not significantly change. Because of the known association between clozapine treatment and OCS, we conducted additional group-comparisons in the subset of patients without clozapine treatment. Results of this sensitivity analyses did not significantly differ from whole sample analyses.

Subsequently, in an explorative approach, we evaluated whether differences in the level of negative symptoms remained stable over the 3-year follow-up period. Patients with complete data on the PANSS negative symptoms subscale at both assessments (n=503) were included in this analyses. Of the original sample 152 patients could not be included because of missing data. Cluster analyses, using baseline data, were repeated with this substantially smaller sample and resulted in highly comparable clusters to those identified using the initial dataset of n=655. As a result of the substantial smaller sample with complete data at 3 year follow-up, the OCShigh/MF cluster consisted of a relatively small number of cases (n=21). For reasons of completeness we included this group in our analyses, but readers should be aware that because of this small sample size results of the OCShigh/MF cluster should be interpreted with caution (see table 1 supplementary material). Figure 1 shows the mean PANSS negative scores per cluster at baseline and follow-up. Correcting the analyses for gender, IQ and clozapine use did not change those result significantly. The uncorrected results are shown. At follow-up, significanly lower negative symptom severity of the OCSmild/HF group compared to the two PF groups at baseline were no

longer apparent. The OCSmild/PF group only showed remaining significantly higher PANSS negative scores compared to the OCSneg/HF group.

Comparing PANSS negative scores at baseline and follow-up per cluster, both HF groups showed significant higher scores at follow up (OCSneg/HF: difference between means= -0,59, SD= 3,59, p=0,016 OCSmild/HF group: difference between means=-1,61, SD= 4,03, p=0,013). The OCSmild/PF group showed significantly lower scores at follow up (difference between means= 1,74, SD= 4,05, p=0,018). However, results did not withstand Bonferroni correction.

4. Discussion

4.1. General discussion

The aim of the current study was to replicate findings of a cluster analyses conducted by Lysaker et al. (2004) based on measures of OCS and social functioning, which resulted in different OCS/schizophrenia groups. Furthermore we aimed to repeat comparisons between these groups on executive functioning, sustained attention and negative symptom severity. It should be acknowledged that due to the fact that GROUP was not specifically designed as a replication study, observed differences in results might partly be explained by differences in assessment instruments (see elaborated discussion below). Our results partly support Lysaker's findings. By using the same cluster analysis as Lysaker et al. (2004) we also found the 4 cluster solution to be optimal. Unfortunately, this solution did not yield the proposed 4 groups differing in functioning and OCS status. Therefore, we used the 5-cluster solution, which resulted in more comparable groups to the study by Lysaker et al. (2004): a OCSneg/PF, OCSneg/HF, OCSmild/PF and OCSmild/HF groups and a fifth group, with high Y-BOCS scores and moderate functioning. In contrast to the original study, mean OCS symptom severity in our sample was considerably lower. Whereas in the sample of Lysaker et al. 32% of patients reported OCS with a Y-BOCS score of 20, only 21% of the current sample reported OCS with a mean score of 12. Nevertheless, similar to Lysaker et al. (2004), we were able to distinguish two different groups of patients with a

psychotic disorder and comorbid OCS – one with mild OCS and relatively good social functioning and one with mild OCS and relatively poor social functioning. Besides differences in sample characteristics, differences in the assessment of social functioning might have affected the results of the cluster analyses. Lysaker et al. used the QoL to assess psychosocial functioning, whereas the SFS was used in GROUP. Although both instruments measure comparable aspects of social functioning (e.g. interpersonal relations, vocational functioning/occupation, common activities/recreation) (Birchwood et al., 1990; Heinrichs et al., 1984), the QoL focusses more on subjective wellbeing, whereas the SFS focusses more on objective well-being. We are not aware of a study directly comparing both instruments, to estimate the potential difference in results. Regarding comparisons between groups on executive functioning and sustained attention, contrary to our hypothesis we did not find significant groups differences. Hence, we could not replicate poorer performance of the OCS/PF group compared to the other groups reported by Lysaker et al. (2004). The addition of the task measuring processing speed, only resulted in lower scores of OCSmild/PF group compared to the OCSneg/HF group. Again, it has to be noted, that observed differences with results reported by Lysaker et al., (2004) might be due to differences in applied assessment instruments. Unfortunately, the Wiscounsin Card Sorting Test, used by Lysaker et al. (2004) was not included in the GROUP-assessment battery. Executive functioning, more specifically cognitive flexibility was measured with the Response Shifting Task in the current study.

In line with our second hypothesis group-comparisons on negative symptom severity revealed that the OCSmild/HF group showed less severe negative symptoms than the two poor functioning groups (the OCSmild/PF and the OCSneg/PF). The OCSmild/PF showed more negative symptoms compared to the two high functioning group. Therefore, in accordance with Lysaker et al. (2004) we found evidence for a subgroup with OCS, high functioning and less severe negative symptoms. In an explorative approach we subsequently investigated whether observed differences in negative symptom severity remained stable over a 3-year period. Results showed that the OCSmild/PF group only showed remaining higher negative symptom severity compared to the OCSneg/HF group, while significant differences between the OCSmild/HF group and the two PF

groups were lost at follow-up. These results do not support the hypothesis that the OCSmild/HF group would show a milder course of illness, expressed by a consistent low score of negative symptom severity at follow-up or any other symptom domains. Hence we did not find evidence for the proposed possibility by Lysaker et al. (2004) that the presence of a group with OCS and better functioning, despite equivalent levels of neurocognitive function might suggest that OCS "have some protective function for persons with schizophrenia who do not have severe neurocognitive deficits". Since the study of Lysaker et al. (2004) has been published, an increasing number of studies has investigated the association between the presence of comorbid OCS and functioning. Several findings have suggested a possible dual impact of OCS on functioning, with mild OCS being associated with better functioning and severe OCS with poorer functioning (de Haan et al., 2013; Tonna et al., 2016a, b). However, Kontis et al., (2016) found a positive association between OCS and social functioning, independent of cognitive functioning and the severity of OCS (Kontis et al., 2016). Other recent studies indicated a negative association with social and vocational functioning, even with relatively mild OCS severity (Schirmbeck et al., 2016b) or no associations (Grover et al., 2017). In line with these inconsistent findings, our cluster analyses results in two groups with mild OCS severity, one with relatively good social functioning and one with relatively poor social functioning. Furthermore, the group with high OCS severity showed moderate function. Hence, we cannot draw general conclusions on the association between the presence of comorbid OCS severity and implications on social functioning, associated clinical impairment or implications for the prospective course. Both cluster analyses suggest that different subgroups of comorbid patients exists, those with high and those with lower social functioning. Apart from associations with negative symptoms, future studies should further investigate possible underlying factors, including a more comprehensive assessment of different cognitive domains, dosage of antipsychotic treatment, environmental factors (e.g. social support) and patient characteristics (e.g. coping strategies). More prospective studies are needed to investigate stability of these clusters and the course of associated variables, particularly as recent findings suggest significant fluctuation and covariation in OCS severity and symptoms of psychosis over time (Schirmbeck et al., 2018)

4.2. Strengths and limitations

The GROUP cohort is a large cohort representing the general patient population with non-affective psychotic disorders and has been assessed with a comprehensive test-battery, including OCS, cognitive functioning and social functioning. Although not specifically designed to replicate the study by Lysaker et al. (2004), GROUP offered the great opportunity to perform a replication approach following most of the original design in a large sample with cross-sectional and longitudinal assessments. With a sample size of 655, we achieved enough power (1-ß=.80) to detect effect sizes as small as f=0.15. Compared to the study by Lysaker et al., (n=66), we would have been able to detect much smaller effects. Therefore, negative results in our study are not likely explained by a type II error. The large sample improves generalizability to the patient population with psychotic disorders. Replication of scientific results is essential. Too few replication studies are performed, while this is a crucial step in the evaluation of scientific results, providing information on stability and generalizability of its conclusions. The longitudinal design of GROUP allowed us to evaluate stability of results after 3-years. However, several limitations should be noted. Differences in patient sample and applied instruments between the current study and Lysaker et al. (2004), addressed earlier, may account for differences in result. In comparison to the sample investigated by Lysaker et al. (2004), the current sample showed less severe OCS, positive and negative symptoms and consisted of much younger participants and included females. Furthermore, no reliable information was available on dosage of antipsychotic treatment. We tried to account for the assumed pro-obsessive effect of particularly clozapine by including a sensitivity analyses, excluding all patients with clozapine treatment.

4.3. Summary

This study is a replication study of a cluster analyses conducted by Lysaker et al. (2004) in a large representative sample of patients with psychotic disorders. The orinigal study found four subgroups of patients with schizophrenia according to the presence of comorbid OCS and the level of social functioning (Lysaker et al., 2004). When chosing a 5-cluster solution the current study identified similar subgroups, including a group with OCS and relatively poor social functioning and a group with OCS and relatively high social functioning. In line with Lysaker et al., the group with OCS and high functioning showed less negative symptoms compared to the groups with poor functioning. However, these differences did not persist at 3-year follow-up. Furthermore, although the large sample provided sufficient statistical power we were not able to replicate that the group with OCS and poorer social functioning showed higher deficits in executive functioning or sustained attention compared to the other groups. Taken together, our results support the assumption that co-morbid OCS can have different implications for different subgroups of patients with psychotic disorders. In some patients OCS seem to be associated with less severe other problems. However, we did not find evidence for a benificial course of illness in this group. Future prospective studies are needed to investigate stability of proposed clusters and apply broader assessment of associated clinical variables.

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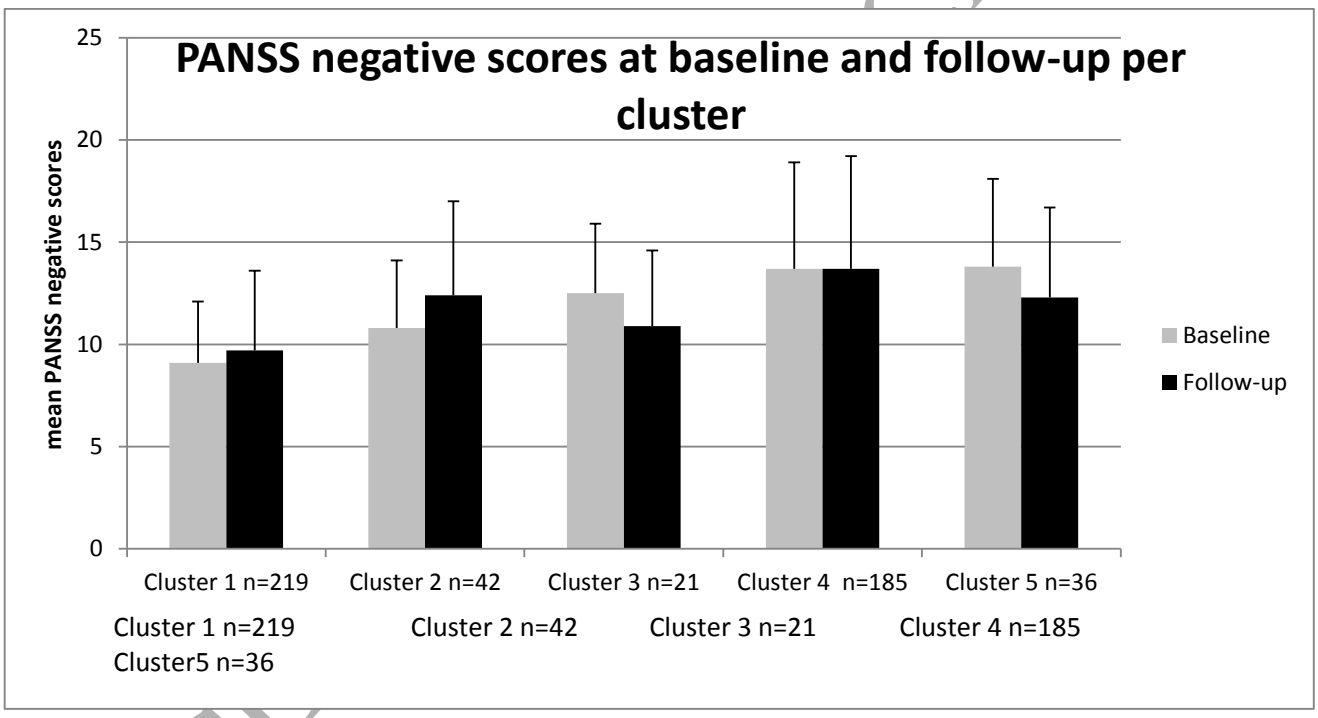

Figure 1 shows the mean PANSS negative scores per cluster at baseline and follow-up.

Table 1 Demografic variables (mean)	Cluster 1 OCSneg/HF (n=276)	Cluster 2 OCSmild/HF (n=52)	Cluster 3 OCShigh/MF (n=36)	Cluster 4 OCSneg/PF (n=241)	Cluster 5 OCSmild/PF (n=50)	F, df	P<
Y-BOCS Total[a]	0.1 ± 0.4	8.0 ± 2.2	19.8 ± 4.3	0.1 ± 0.5	10.0 ± 3.0	$F_{4,654}$ = 2042.2	0.0005
SFS Total[b]	120.6 ± 4.8	116.5 ± 5.1	108.5 ± 8.8	105.1 ± 6.2	102.2 ± 6.2	$F_{4,654}$ = 290.8	0.0005
Age	27.2 ± 7.2	26.6 ± 6.2	27.1 ± 6.3	27.9 ± 8.0	27.1 ±6.1	$F_{4,654}$ =0.5	NS
Male%	69.9	73.1	83.8	82.2	80.0	$X^2_{4,659}$ = 12.7	0.013
Education%						$X^2_{8,655}$ = 34.9	0.001
Primary school	5.4	13.3	19.4	14.9	14.0		
Secondary school	57.6	63.5	58.3	66.0	70.0		
Higher education	37.0	23.1	22.2	19.1	16.0		
IQ	102.4 ± 15.8	95.8 ± 13.8	98.1 ± 19.0	96.2 ± 16.9	94.0 ± 14.6	$F_{4,484}$ = 4.9	0.001
Duration of illness(years)	7.4 ± 3.7	8.0 ± 4.1	8.1 ± 3.8	7.7 ± 4.8	8.0 ± 4.1	$F_{4,621}$ = 0.4	NS

Clozapine use % using	7.5	28.8	45.9	22.8	22.0	$X^2_{4, 659}$ = 48.7	0.0005

Table 1: Shows mean SFS and Y-BOCS scores and the demographic characteristics of the 5 clusters. Abbreviations: IQ: Intelligence quotient, OCSneg/HF (no-OCS and high functioning), OCSmild/HF (mild OCS and high functioning), OCShigh/MF (high OCS and moderate functioning), OCSneg/PF (no-OCS and poor functioning), OCSmild/PF (mild OCS and poor functioning), NS: not significant, SFS: Social Functioning Scale, Y-BOCS: Yale Brown Obsessive Compulsive Scale

Table 2: Shows the mean scores and group-differences on the PANSS subscales and investigated cognitive domains at baseline

Results at baseline	Cluster 1 OCSneg/HF (n=276)	Cluster 2 OCSmild/HF (n=52)	Cluster 3 OCShigh/MF (n=36)	Cluster 4 OCSneg/PF (n=241)	Cluster 5 OCSmild/PF (n=50)	F, df	P<
Y-BOCS Total[a]	0.1 ± 0.4	8.0 ± 2.2	19.8 ± 4.3	0.1 ± 0.5	10.0 ± 3.0	$F_{4,654}$ = 2042.2	0.0005
SFS Total[b]	120.6 ± 4.8	116.5 ± 5.1	108.5 ± 8.8	105.1 ± 6.2	102.2 ± 6.2	$F_{4,654}$ = 290.8	0.0005
GAF S[c]	68.6 ± 14.3	57.2 ± 12.7	50.8 ± 16.4	56.9 ± 13.5	47.5 ± 15.3	$F_{4,556}$ = 36.8	0.0005
PANSS scales							
Positive[d]	9.2 ± 3.4	12.0 ± 3.7	14.7 ± 5.1	11.6 ± 4.8	13.4 ± 4.7	$F_{4,645}$ = 25.9	0.0005
Negative[e]	9.3 ± 3.1	11.0 ± 3.5	13.4 ± 4.5	14.1 ± 5.6	14.6 ± 6.1	$F_{4,645}$ = 42.1	0.0005
General[f]	20.5 ± 5.3	24.8 ± 5.2	30.5 ± 7.4	25.6 ± 7.0	28.9 ± 7.3	$F_{4,645}$ = 42.5	0.0005
Cognitive scales							
Digital symbol Coding[g]	9.1 ± 3.3	7.8 ± 3.0	7.8 ± 2.9	7.4 ± 2.7	7.1 ± 2.2	$F_{4,488}$ = 8.9	0.0005
RST accuracy	0.19 ± 0.26	0.15 ± 0.27	0.26 ± 0.33	0.19 ± 0.27	0.17 ± 0.22	$F_{4,621}$ = 1.0	NS
CPT omissions[h]	0.96 ± 1.8	1.21 ± 1.7	2.13 ± 3.0	1.45 ± 2.5	1.77 ± 2.8	$F_{4,691}$ = 3.3	0.011

CPT commisions	1.64 ± 10.0	1.50 ± 4.6	1.53 ± 2.5	2.15 ± 9.7	1.29 ± 3.1	$F_{4,591}$ = 0.2	NS

Abbreviation: CPT: Continuous Performance Test, GAF: General Assessment of Functioning Scale, OCSneg/HF (no-OCS and high functioning), OCSmild/HF (mild OCS and high functioning), OCShigh/MF (high OCS and moderate functioning), OCSneg/PF (no-OCS and poor functioning), OCSmild/PF (mild OCS and poor functioning), PANSS: Positive and Negative Syndrome Scale, NS: not significant, RST: Response Shift Task, SFS: Social Functioning Scale, Y-BOCS: Yale Brown Obsessive Compulsive Scale

[a]Cluster 3 > cluster 5 > Cluster 2 > ,cluster 1,cluster 4, P < 0.0005

[b]Cluster 1 > Cluster 2 > Cluster 3 > Cluster 4, P < 0.0005; Cluster 3 > cluster 4, P=0.010; Cluster 4 > Cluster5, P=0.011

[c]Cluster 1 > Cluster 2, 3, 4, 5, P < 0.0005; Cluster 2, 4 > Cluster 5, P < 0.05

[d]Cluster 2, 3, 4, 5 > Cluster 1, P < 0.0005; Cluster 3> Cluster 4, P < 0.0005; Cluster 3 > Cluster 2, P = 0.023

[e]Cluster 4, 5 > Cluster 1, 2, P < 0.001; Cluster 3 > Cluster 1, P < 0.0005

[f]Cluster 3 > Cluster 1, 2, 4, P < 0.0005; Cluster 5> cluster1, P < 0.0005; Cluster 5 > Cluster 4, P = 0.010; Cluster 5 > Cluster 2, P=0.011; Cluster 2, 4 > Cluster 1, P < 0.0005

[g]Cluster 1 > Cluster 4, 5, P < 0.001

[h]Cluster 3 > Cluster 1, P = 0.066